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EXAMINER

1SN2/0915

FLEHR HOHBACH TEST ALBRITTON  
AND HERBERT  
FOUR EMBARCADERO CENTER  
SUITE 3400  
SAN FRANCISCO CA 94111

ATTY/DOCKET NO.	ART UNIT	PAPER NUMBER
1804	17	1804

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This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

### OFFICE ACTION SUMMARY

Responsive to communication(s) filed on 5/27/97

This action is FINAL.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claims

Claim(s) 26, 27, 32-51 is/are pending in the application.  
Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

Claim(s) \_\_\_\_\_ is/are allowed.

Claim(s) 26, 27, 32-51 is/are rejected.

Claim(s) \_\_\_\_\_ is/are objected to.

Claim(s) \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All  Some\*  None\* of the CERTIFIED copies of the priority documents have been

received.  
 received in Application No. (Series Code/Serial Number) \_\_\_\_\_  
 received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

Notice of Reference Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). 14, 16

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

-SEE OFFICE ACTION ON THE FOLLOWING PAGES--

This application should be reviewed for errors.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-25 and 28-31 have been cancelled; claims 32-51 are newly added; claims 26, 27 and 32-51 are active and examined in this Office Action.

The rejection of claim 26 under 35 USC 112, first paragraph, regarding the transplantation of any and all stem cell progeny is withdrawn.

The rejection of claim 27 under 35 USC 112, first paragraph, regarding the transplantation of genetically modified stem cell progeny is maintained. Applicant's arguments, filed May 27, 1997, have been considered but not found to be persuasive. Applicants have argued that the examiner's arguments are directed to a lack of credible utility for the claimed invention. However, no rejection was made under 35 USC 101 and arguments directed to utility will therefore not be addressed.

Applicants have argued that their methods of in vitro proliferation provide a ready source of cells that can easily be induced to proliferate in vitro and thus become readily amenable to genetic modification. However, such arguments do not address the issue of longevity of expression and if sufficient levels can be expressed for the requisite length of time to achieve any therapeutic effect. Such issues were readily identified by Friedman and the issues remain problematic.

Claim 38 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not provide support for the invention as claimed. The specification fails to disclose that any subsequent passage contains a percentage of multipotent stem cells that is at least ten fold

higher than that of said neural cells obtained in (a). The cited location in the specification does not provide support for such claimed cell numbers. Further, the specification fails to disclose or contemplate methods for measuring the number of multipotent stem cells obtained at any particular passage.

The rejection of claim 26 under 35 USC 102(a) as being anticipated by Lubetzke is maintained. Applicants have argued that the reference is concerned with transfection of enriched oligodendrocyte cultures and enriched O-2A cultures and that Lubetzke do not teach a method for inducing the proliferation of multipotent neural stem cells capable of producing progeny that are capable of differentiating into neurons, astrocytes and oligodendrocytes. However, the claim is directed to methods of transplantation of neural stem cell progeny and O-2A cells are neural stem cell progeny and are capable of giving rise to astrocytes and oligodendrocytes. Further, although the neural cell population derived from day old rat brains was 70-80% pure O-2A cells, 20-30% were "other" cells and since the cell population was derived from brains, the transplanted cell population presumably contained some stem cells. Differentiation into astrocytes, neurons and oligodendrocytes is an inherent property of stem cells and therefore Lubetzke is correctly applied. The transplanted cell population was multipotent. Lubetzke discloses that the progenitor cells were induced to proliferate on page 67, "Cell cultures" since PDGF was added.

The rejection of claim 27 under 35 USC 103 as being unpatentable over Lubetzki and Gage is maintained. The examiner disagrees with applicant's arguments that "neuron=nerve cell". A neuron is a type of nerve cell. Not all nerve cells are neurons.

Claims 32-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lubetzki as applied to claim 26 above and further in view of Olson and Pezzoli. Lubetzke differs from the claims in that the reference fails to disclose addition of other

growth factors. Olson discloses that other growth factors such as bFGF, aFGF and TGFs can stimulate growth of fetal brain tissue. Regarding claims 33 and 35, the use of epidermal growth factor is an obvious variation of the addition of other growth factors. Pezzoli discloses the addition of EGF resulted in an increase in the number of preserved neurons. Pezzoli discloses on page 285 that EGF may have a mitogenic activity in vivo not only on fetal or newborn animals cells but also on animal cells. In view of the teachings of Pezzoli, it would have been obvious to add EGF to the culture medium.

Regarding claim 36, (a) does not claim treatment with serum and the phrase "substantially free" is the standard culture condition, lacking evidence to the contrary.

Regarding claim 37, repetitive rounds of cell culture of primary cell cultures is routinely done by those of ordinary skill in the art.

Regarding claims 38-40, Lubetzke discloses that the cells were capable of differentiating and in view of the initiation of the procedure with a brain-derived cell population, included neural stem cells in the transplant.

Regarding claims 41-47, the site of transplantation depends upon the site of injury and Gage and Lubetzki teach the transplantation of cells.

Regarding claims 48-51, the type of neural tissue transfected is obvious over the transfection of mature and day old cells of Lubetzki.

It would have been obvious to one of ordinary skill to modify the method of Lubetzke, Gage and Pezzoli by culturing the cells prior to transplantation view of the teachings of Lubetzki that the cells were cultured in the presence of growth factors capable of stimulating proliferation and differentiation. One of ordinary skill would have had a reasonable expectation of success

in view of Lubetzki and the motivation to combine the references is found therein.

Accordingly, the modification of the method of Lubetzki and Gage by adding other growth factors as suggested by Pezzoli was within the ordinary skill in the art at the time the claimed invention was made. From the teachings of the references, it is apparent that one of ordinary skill would have had a reasonable expectation of success in producing the claimed invention and the invention as a whole is prima facie obvious.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO FAX center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (30 November 15, 1989). The CM1 official Fax Center number is (703) 305-3014 or (703) 305-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Suzanne Ziska, Ph.D., whose telephone number is (703) 308-1217. In the event the examiner is not available, the examiner's supervisor, Jasemine Chambers, Ph.D., may be contacted at phone number (703) 308-3153.

  
SUZANNE E. ZISKA  
PRIMARY EXAMINER  
GROUP 1800